Stereoselective Syntheses of all the Possible Stereoisomers of Coronafacic Acid

Raku Watanabe,[a] Nobuki Kato,*[b] Kengo Hayashi,[b] Sho Tozawa,[b] Yusuke Ogura,[c] Shigefumi Kuwahara,[c] and Minoru Ueda*[a, b]

An efficient and stereoselective syntheses of all the possible stereoisomers of coronafacic acid (CFA) has been developed. The stereochemistries of C3a and C7a were controlled in a diastereoselective Diels-Alder type cycloaddition using a chiral auxiliary. CFA and 6-*epi*-CFA were synthesized by hydrogenation of a common intermediate. During the synthesis of 6-*epi*-CFA, we established that its *cis*-fused configuration is important for the introduction of C4-C5 double bond by dehydration. This report is the first practical synthesis of both 6-*epi*-CFA, and its enantiomer.

1. Introduction

Jasmonate, an oxylipin-type plant hormone, plays important roles in the life cycle of plants,[1–3] and (+)-(3*R*, 7*R*)-jasmonoyl-L-isoleucine (JA-Ile, **1**)[4] is a significant endogenous bioactive jasmonate which causes myriad of plant biological responses including those associated with defense, response to wounds, fertility, senescence, secondary metabolite production, and growth inhibition (Figure 1). Hormone **1** has been used as an important chemical tool in the field of jasmonate biology. However, (3*R*, 7*R*)-JA-Ile is unsuitable for use in biological studies due to its tendency to isomerize into the biologically inactive (3*R*, 7*S*)-form,[4] and therefore coronatine (COR, **2**), a more stable structural and biological mimic of JA-Ile, is generally used as a chemical tool in jasmonate research instead.[5,6]

Recently, we found that NOPh (**3**), an oxime derivative of COR, caused defense response against pathogenic infection without undesired biological responses such as growth inhibition.[7,8] This result is based on a slight difference in the 3D shape of coronatine. Therefore, a chemical library composed of all the possible 16 stereochemical isomers of COR could be useful as a source of useful chemical tool in jasmonate biology. COR is composed of coronafacic acid (CFA, **4**) and unusual amino acid coronamic acid (CMA, **5**). To date, the possible four stereochemical isomers of CMA can be also accomplished by Salaün,[9] Charette,[10] and Toshima & Ichihara,[11] and syntheses of CFA have been accomplished by many groups[12,13] including practical supply by Watson and Ueda.[14,15] However, no report can be found for practical supply of 6-*epi*-CFA (**6**) and its enantiomer (*ent*-**6**) (Scheme 1). Here, we report the first syntheses of **6** and *ent*-**6**. We synthesize both of CFA and 6-*epi*-CFA from the common intermediates (**9**) by switching the stereoselectivity in hydrogenation (Scheme 1).

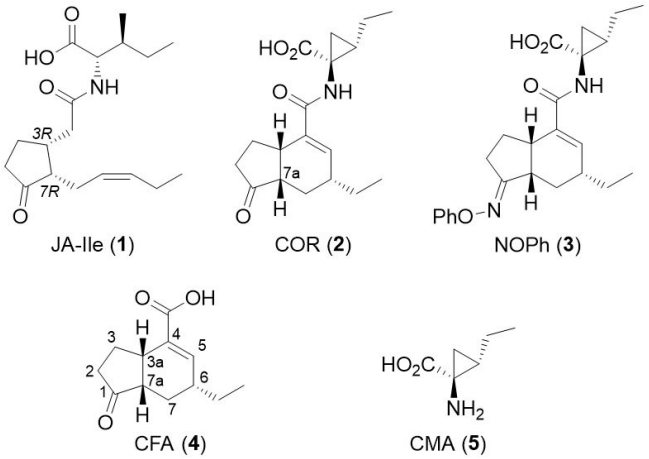

Figure 1. JA-Ile (**1**), COR (**2**), NOPh (**3**), CFA (**4**) and CMA (**5**).

We previously obtained enantiopure samples of **4** and *ent*-**4** by separation of (±)-**4**, but this is not practical on large scales. Therefore, we planned to develop practical stereoselective syntheses of all stereoisomers of **4** based on our previous synthetic route.[16]

Enol **7** was proposed as a possible starting material for all stereoisomers of **4** (Scheme 1). A diastereoselective Diels-Alder type reaction between **7** and **8**/*ent*-**8** could be used to establish the desired absolute configurations at C3a and C7a, and the stereochemistry at C6 could be catalytically controlled in a stereoselective hydrogenation – we have previously reported that the palladium-catalyzed hydrogenation of **9** selectively

[a] *R. Watanabe, Prof. M. Ueda*
Graduate School of Life Science, Tohoku University, 6–3, Aramaki-Aza-Aoba, Aoba-ku, Sendai 980-8578, (Japan)
E-mail: minoru.ueda.d2@tohoku.ac.jp
[b] *Dr. N. Kato, K. Hayashi, S. Tozawa, Prof. M. Ueda*
Graduate School of Science, Tohoku University, 6–3, Aramaki-Aza-Aoba, Aoba-ku, Sendai 980-8578, (Japan)
E-mail: nobuki.kato.e7@tohoku.ac.jp
[c] *Dr. Y. Ogura, Prof. S. Kuwahara*
Laboratory of Applied Bioorganic Chemistry, Graduate School of Agricultural Science, Tohoku University, Sendai 980–8572, (Japan)

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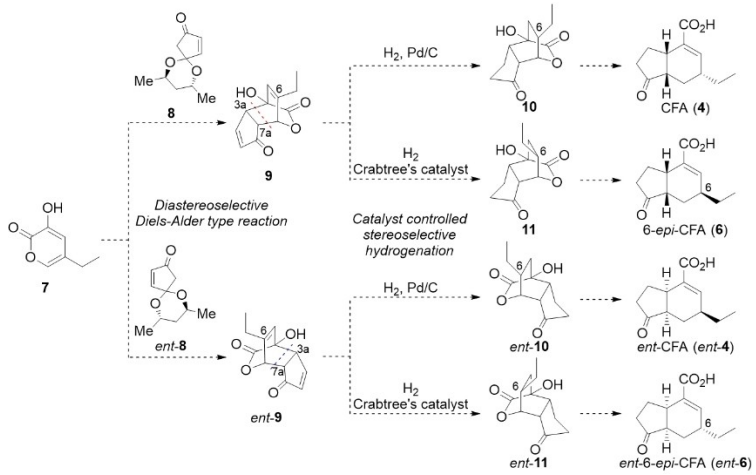


Scheme 1. Systematic strategy used to synthesize all stereoisomers of **4**.

afforded **10** having the naturally occurring C6 configuration,[16] but by using Crabtree's catalyst (which coordinates to the lactone carbonyl group), **11** with the unnatural C6 configuration was obtained.[17] The resulting **11** can be converted to 6-*epi*-CFA (**6**). The enantiomers *ent*-**4** and *ent*-**6** were obtained from *ent*-**9** using the same method.

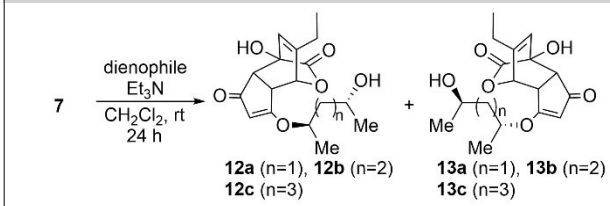
2. Results and Discussion

At first, we investigated the diastereoselective Diels-Alder type reaction (Table 1).[18] Using a variety of chiral dienophile acetals (**14**, **8**, **15**),[19] the ring-opened compounds (**12a–c** and **13a–c**) were obtained - the result of Diels-Alder type reaction and subsequent cyclic acetal opening by β-elimination (entries 1–3). Only the *exo* cyclization products were obtained; no *endo* cyclization products were observed.[20] The best yield and selectivity was obtained with the 6-membered cyclic acetal **8** (entry 2).

Next, we examined the effect of temperature on the reaction outcome (Table 2). When the reaction was conducted at −20 °C, the selectivity decreased compared with at room temperature, though we do not have any reason to explain the decrease in selectivity (entries 1 and 2). On the other hand, conducting the reaction at −40 °C for 5 d gave the desired product **12b** in 64% yield with higher selectivity (entry 3). The desired compound **12b** and its diastereomer **13b** were readily separable by silica-gel column chromatography.

The stereoselectivity of this reaction can be explained by the model depicted in Figure 2. The six-membered ring of compound **8** can exist in two possible conformations (**A** and **B**), of which **A** predominates as **B** is destabilized by steric repulsion

Table 1. Screening of chiral auxiliaries on the diastereoselective Diels-Alder type reaction.



Entry	Dienophile	Result	12:13
1	**14**	**12a** (42%), **13a** (33%)	1.3:1
2	**8**	**12b** (59%), **13b** (17%)	3.5:1
3	**15**	**12c** (56%), **13c** (21%)[a]	2.7:1[b]

[a] The yield was determined by ^{1}H NMR. [b] The ratio was determined by ^{1}H NMR.

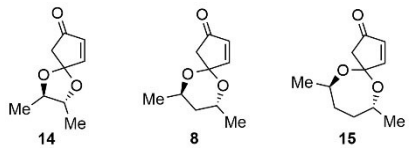
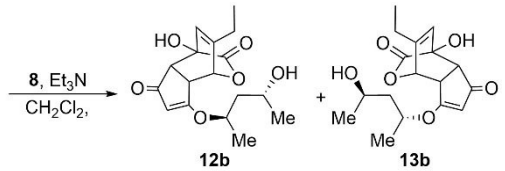


Table 2. Effects of temperature on the diastereoselective Diels-Alder type reaction.



Entry	Condition	Result	12b:13b
1	rt, 24 h	**12b** (59%), **13b** (17%)	3.5:1
2	−20 °C, 40 h	**12b** (52%), **13b** (18%)	2.9:1
3	−40 °C, 5 d	**12b** (64%), **13b** (14%)	4.6:1

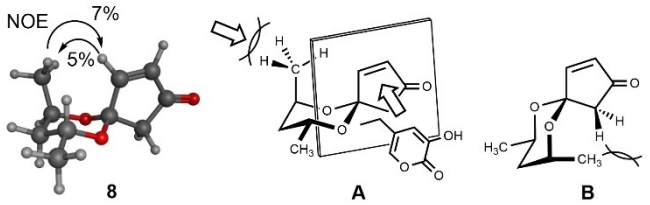
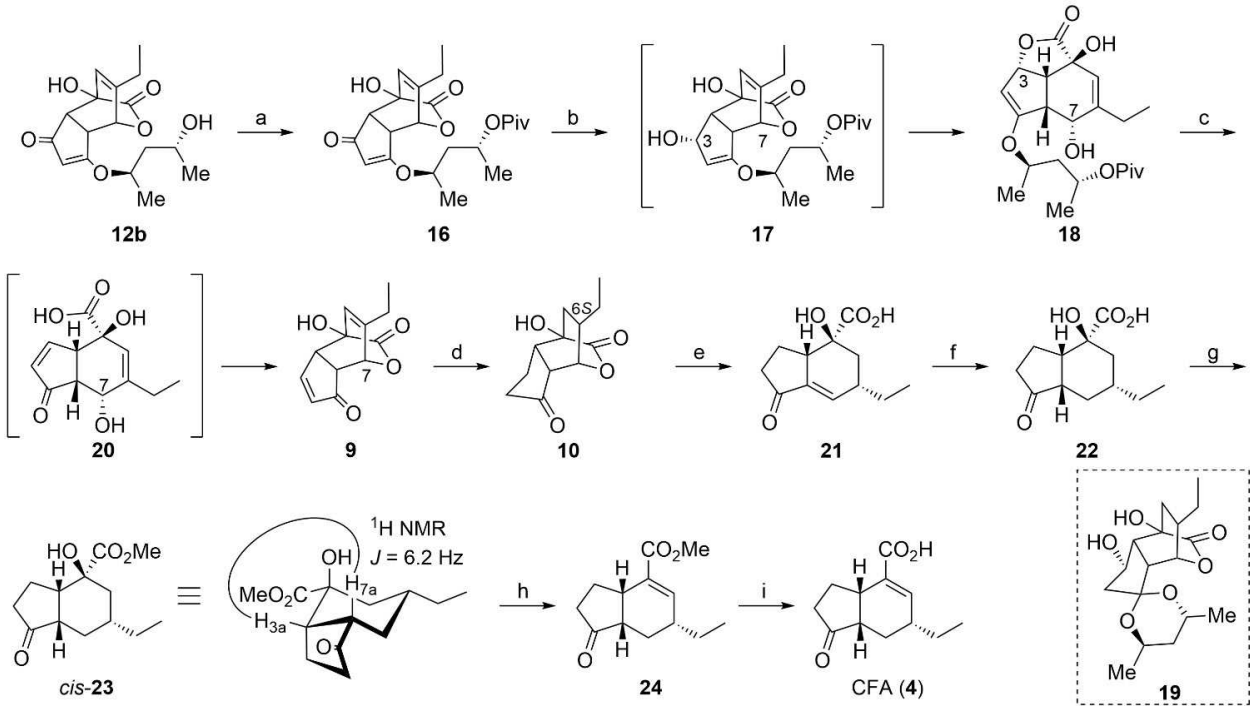


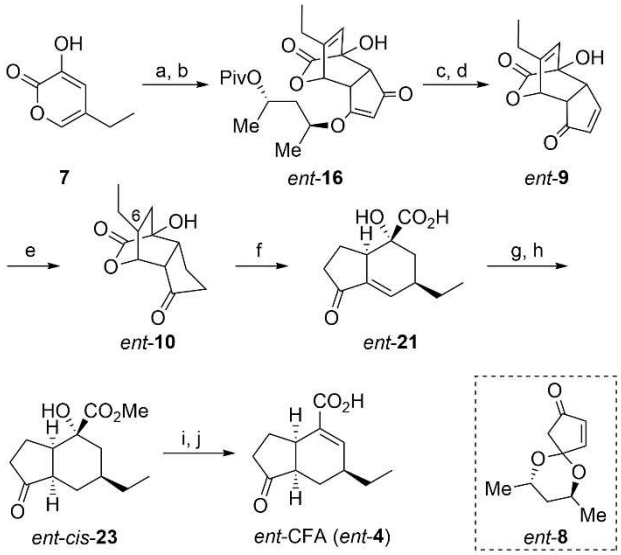
Figure 2. Proposed model for observed facial selectivity.



Scheme 2. *Reagents and conditions*: (a) PivCl, pyridine, quant.; (b) BH_3·THF, THF, 0 °C; HCl aq., 93%; (c) TFA, THF, 0 °C, 75%; (d) H_2, Pd/C, toluene, **10** (71%), **11** (23%); (e) NaOMe, MeOH; (f) H_2, Pd/C, MeOH; (g) $TMSCHN_2$, benzene MeOH, 70% (3 steps); (h) $POCl_3$, pyridine, 0 °C, 91%; (i) HCl, H_2O, reflux, quant.

between the axial methyl and cyclopentenone methylene groups. This is consistent with NOE studies which revealed a correlation between the axial methyl group and β-proton of the cyclopentenone in **8**. Attack of conformation **A** by diene **7** is anticipated to proceed from the equatorial methyl face opposite the axial methyl group.

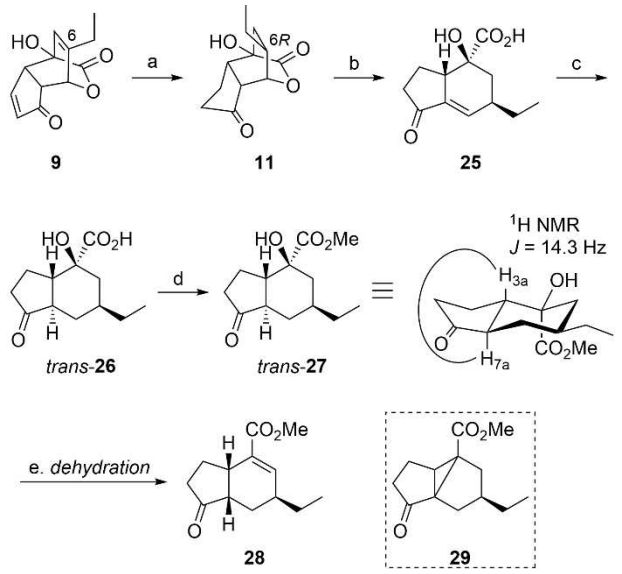
Our synthesis of CFA (**4**) is summarized in Scheme 2. Diels-Alder type reaction product **12b** was treated with PivCl and pyridine to afford **16**. BH_3 reduction of the ketone of **16**, and spontaneous transesterification between the C7 and C3 hydroxy groups gave lactone **18**. In the BH_3 reduction of **12b**, the desired lactone was not obtained and instead the undesired **19** was generated as a result of conjugate addition of hydroxy group and subsequent reduction of ketone. Lactone **18** was treated with TFA to afford α,β-unsaturated enone **9**, the common intermediate of **4** and **6**, via hydroxy carboxylic acid **20**. Hydrogenation of **9** with Pd/C resulted in stepwise reductions to give the desired monoketone **10** (having the naturally occurring 6*S* configuration) and its C6 epimer **11** in yields of 71% and 23% respectively. Fortunately, **10** and **11** were easily separated by silica-gel column chromatography. Ring-opening of **10** by β-elimination and subsequent hydrogenolysis afforded *cis*-**23**. The observed H_{3a}-H_{7a} coupling constant ($^3J_{3a,7a} = 6.2$ Hz) is consistent with a *cis*-fused configuration. Finally, methyl esterification of *cis*-**23**, dehydration of the resulting **24** with phosphorus oxychloride, and hydrolysis under acidic conditions gave optically pure CFA (**4**) in 17 steps and 7% overall yield from **12**. *ent*-CFA (*ent*-**4**) was also obtained from **7** and *ent*-**8** by the same method (Scheme 3). The optical purities of **4** and *ent*-**4** were determined by chiral HPLC analyses



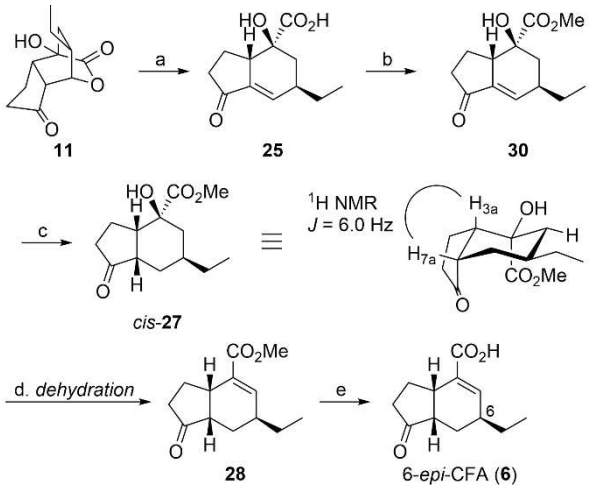
Scheme 3. *Reagents and conditions*: (a) *ent*-**8**, Et_3N, CH_2Cl_2, −60 °C, 63%; (b) PivCl, pyridine; (c) BH_3·THF, THF, 0 °C; HCl aq.; (d) TFA, THF, 0 °C, 41% (3 steps); (e) H_2, Pd/C, toluene, 68%; (f) NaOMe, MeOH; (g) H_2, Pd/C, MeOH, 68%; (h) $TMSCHN_2$, benzene MeOH; (i) $POCl_3$, pyridine, 0 °C, 67% (4 steps); (j) HCl, H_2O, reflux, quant.

on a Chiralpak IA after methyl esterification with trimethylsilyl diazomethane. Chiral HPLC analysis of synthetic **4** and *ent*-**4** gave optical purities of > 99.5% ee.

Next, we synthesized 6-*epi*-CFA (**6**) (Scheme 4). Hydrogenation of the common intermediate **9** using Crabtree's catalyst proceeded from the lactone side as expected, to give the



Scheme 4. *Reagents and conditions*: (a) H_2, [Ir(cod)(py)(PCy_3)]PF_6, CH_2Cl_2, **11** (76%), **10** (16%); (b) NaOMe, MeOH; (c) H_2, Pd/C, MeOH; (d) $TMSCHN_2$, benzene MeOH, 70% (3 steps); (e) see, Table 3.



Scheme 5. *Reagents and conditions*: (a) NaOMe, MeOH; (b) $TMSCHN_2$, benzene MeOH; (c) H_2, Pd/C, MeOH, 70% (3 steps); (d) see, Table 4; (e) HCl, H_2O, reflux, quant.

desired 6*R* ketone **11** stereoselectively. Interestingly, ring-opening by β-elimination, hydrogenation, and methyl esterification afforded *trans*-fused **27** but not the C6 epimer of the *cis*-fused **23**, the intermediate in the synthesis of CFA (**4**). The coupling constant ($^3J_{3a,7a}$ = 14.3 Hz) is consistent with *trans*-configuration. Then, we investigated the dehydration of *trans*-**27** (Table 3). Phosphorus oxychloride (which was used for the synthesis of **4** and *ent*-**4**) was tested first (entry 1). The desired α.β-unsaturated ester **28** was obtained as a result of dehydration and isomerization, though the reaction yield was low. When *trans*-**27** was treated with Martin sulfurane[21] to afford only a trace amount of **28** and cyclopropane **29** (entry 2). Neither the Burgess dehydration reaction[22] nor the Chugaev elimination,[23] (a *syn*-elimination) were efficient either (entries 3 and 4). Although the ketone of *trans*-**27** was masked with an acetal to prevent cyclopropanation, the dehydration reaction was not improved.

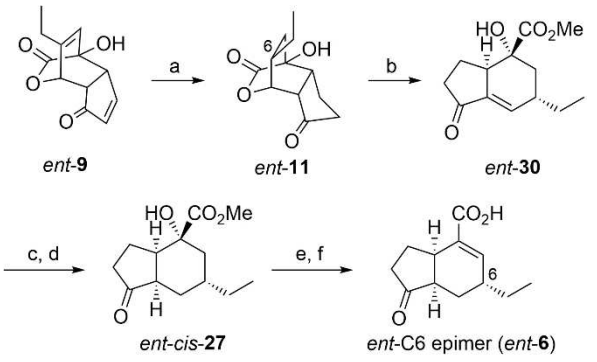
Due to the poor yields obtained for the dehydration of *trans*-**27**, we planned to dehydrate *cis*-**27** (Scheme 5). The hydrogenation of cyclic compounds using Pd/C is known to proceed from the opposite side of the ring to the methoxycarbonyl groups.[24] Therefore, hydrogenation was conducted after methyl esterification to obtain *cis*-**27**. The configuration of *cis*-**27** was determined by the $^3J_{AB}$-based configurational ^{1}H NMR analysis ($^3J_{3a,7a}$ = 6.0 Hz). Then, we investigated the dehydration of *cis*-**27** (Table 4). The highest yield was obtained using phosphorus oxychloride (entry 2). Finally, hydrolysis under the acidic condition gave 6-*epi*-CFA (**6**) stereoseletively in 17 steps and 7% overall yield from **12**. *ent*-6-*epi*-CFA (*ent*-**6**) was also obtained from *ent*-**9** by the same method (Scheme 6). The optical purities of **6** and *ent*-**6** were determined by chiral HPLC analyses on a Chiralpak IA after methyl esterification with trimethylsilyl diazomethane. Chiral HPLC analysis of synthetic **6** and *ent*-**6** gave optical purities of > 97% ee.

Table 3. Dehydration of *trans*-**27**.

Entry	Condition	28	29
1	$POCl_3$, pyridine, rt, 12 h	21%	0%
2	Martin sulfurane, CH_2Cl_2, rt, 24 h	trace	12%
3	Burgess reagent, toluene, reflux, 6 h	25%	6%
4	1) NaH, imidazole, CS_2, THF; MeI, 0 °C 2) toluene, reflux, 20 h	trace	trace

Table 4. Dehydration of *cis*-**27**.

Entry	Condition	28	29
1	Martin sulfurane, CH_2Cl_2, rt, 1 h	0%	78%
2	$POCl_3$, pyridine, rt, 7 h	87%	10%
3	$SOCl_2$, pyridine, 0 °C, 3 h	54%	8%
4	Burgess reagent, toluene, reflux, 1 h	55%	32%



Scheme 6. *Reagents and conditions*: (a) H_2, [Ir(cod)(py)(PCy_3)]PF_6, CH_2Cl_2, 73%; (b) NaOMe, MeOH; (c) $TMSCHN_2$, benzene MeOH, 91% (2 steps); (d) H_2, Pd/C, MeOH, 98%; (e) $POCl_3$, pyridine, 0 °C, 75%; (f) HCl, H_2O, reflux, quant.

3. Conclusions

Efficient and stereoselective syntheses of all four possible stereoisomers of CFA have been developed; key reactions are the diastereoselective Diels-Alder type reaction (to establish the desired absolute configuration) and the catalyst-controlled stereoselective hydrogenation. Our method is stereoselective and the desired stereoisomers were obtained without using the cumbersome separations of stereoisomers. Our method allows practical supply of 6-*epi*-CFA and the enantiomer. Studies towards the generation of a chemical library consisting of all the possible 16 stereochemical isomers of COR, a useful chemical tool in jasmonate chemical biology, are underway.

Experimental Section

General

All chemical reagents and solvents were obtained from commercial suppliers (Kanto Chemical Co. Ltd., Wako Pure Chemical Industries Co. Ltd., Nacalai Tesque Co. Ltd., Tokyo Chemical Industry Co. Ltd., Sigma-Aldrich Co. LLC., GE Healthcare) and used without further purification. All anhydrous solvents were either dried by standard techniques and freshly distilled before use, or purchased in anhydrous form and used as supplied. Reversed-phase high-performance liquid chromatography (HPLC) was carried out on a PU-4180 plus pump equipped with UV-4075 and MD-4010 detectors (JASCO, Tokyo, Japan). 1H and 13 C NMR spectra were recorded on a JNM-ECS-400 spectrometer (JEOL, Tokyo, Japan) in deuterated chloroform using TMS as an internal standard. Fourier transform infrared (FT/IR) spectra were recorded on an FT/IR-4100 (JASCO, Tokyo, Japan). High-resolution (HR) electrospray ionization (ESI)-mass spectrometry (MS) analyses were conducted using a microTOF II (Bruker Daltonics Inc., Billerica, MA). Optical rotations were measured using a JASCO P-2200 polarimeter (JASCO, Tokyo, Japan). Flash chromatography was performed on an Isolera system (Biotage Ltd., North Carolina, US). TLC analyses were performed on Silica gel F254 (0.25 mm or 0.5 mm, MERCK, Germany) or RP-18F254S (0.25 mm, MERCK). $SiO_2/K_2CO_3/H_2O$ is a homogeneous mixture of 400 g of SiO2, 40 g of K_2CO_3 and 120 mL of water. All reactions were carried out under air unless stated otherwise.

Synthesis of Chiral Acetal 8

To a solution of 4-cyclopentene-1,3-dione (2.77 g, 28.8 mmol) and (2*R*,4*R*)-(−)-2,4-pentanediol (2.01 g, 19.3 mmol) in toluene (120 mL) was added TsOH·H_2O (731 mg, 3.84 mmol). The reaction mixture was refluxed with stirring. After 1 h, the mixture was concentrated *in vacuo* to give a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1) to give **8** (1.99 g, 6.14 mmol, 59%) as a colorless oil. $[\alpha]_D^{23}$ + 16.2 (*c* 1.0, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.47 (d, *J* = 5.9 Hz, 1H), 6.20 (d, *J* = 5.9 Hz, 1H), 4.18 (dquintet, *J* = 7.7 Hz, 6.3 Hz, 1H), 4.06 (dquintet, *J* = 8.2, 6.3 Hz, 1H), 2.68 (d, *J* = 17.8 Hz, 1H), 2.59 (d, *J* = 17.8 Hz, 1H), 1.75 (ddd, *J* = 13.1, 8.2, 6.3 Hz, 1H), 1.72 (ddd, *J* = 13.2, 7.7, 6.3 Hz, 1H), 1.28 (d, *J* = 6.3 Hz, 3H), 1.27 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR(100 MHz, $CDCl_3$) δ_C 204.7, 157.4, 134.6, 104.8, 65.2, 65.0, 47.2, 39.6, 21.7, 21.3; IR (film); 2975, 2933, 2878, 1727, 1457, 1384, 1340, 1268, 1150, 1024, 795 cm^{-1}; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{10}H_{14}NaO_3$: 205.0835, Found: 205.0833.

Synthesis of Diels-Alder Type Reaction Product 12b

To a solution of **7** (1.46 g, 10.4 mmol) and **8** (2.71 g, 14.9 mmol) in CH_2Cl_2 (70 mL) was added Et_3N (1.5 mL, 10.8 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for 24 h. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1) to give **12b** (1.99 g, 6.14 mmol, 59%) as a colorless oil and the diastereomer **13b** (575 mg, 1.77 mmol, 17%) as a colorless oil; **12b**: $[\alpha]_D^{21}$ −176.0 (*c* 0.75, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.07 (q, *J* = 1.9 Hz, 1H), 5.44 (d, *J* = 0.7 Hz, 1H), 5.05 (t, *J* = 1.9 Hz, 1H), 4.67 (dqd, *J* = 9.3, 6.2, 2.8 Hz, 1H), 4.15 (brs, 1H), 3.94 (dqd, *J* = 10.1, 6.3, 2.8 Hz, 1H), 3.19 (ddd, *J* = 7.5, 1.9, 0.7 Hz, 1H), 2.79 (d, *J* = 7.5 Hz, 1H), 2.32 (dqd, *J* = 16.4, 7.3, 1.9 Hz, 1H), 2.26 (dqd, *J* = 16.4, 7.3, 1.9 Hz, 1H), 1.86 (ddd, *J* = 14.7, 9.3, 2.8 Hz, 1H), 1.70 (ddd, *J* = 14.7, 10.1, 2.8 Hz, 1H), 1.37 (d, *J* = 6.2 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.12 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 202.1, 185.9, 172.8, 145.2, 128.2, 107.4, 77.9, 77.1, 76.4, 63.5, 50.4, 48.2, 45.4, 24.8, 24.5, 20.0, 11.2; IR (film) cm^{-1}: 3419, 2970, 2933, 2883, 1770, 1677, 1579, 1457, 1373, 1341, 1186, 1116, 958, 912; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{17}H_{22}NaO_6$: 345.1314, Found: 345.1314.

13b: $[\alpha]_D^{22}$ + 74.7 (*c* 0.75, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.07 (q, *J* = 2.0 Hz, 1H), 5.44 (d, *J* = 0.4 Hz, 1H), 5.04 (t, *J* = 2.0 Hz, 1H), 4.66 (dqd, *J* = 9.2, 6.4, 2.6 Hz, 1H), 3.94 (dqd, *J* = 10.0, 6.4, 2.8 Hz, 1H), 3.19 (ddd, *J* = 7.2, 2.0, 0.4 Hz, 1H), 2.77 (d, *J* = 7.2 Hz, 1H), 2.32 (dqd, *J* = 17.2, 7.2, 2.0 Hz, 1H), 2.22 (dqd, *J* = 17.2, 7.2, 2.0 Hz, 1H), 1.87 (ddd, *J* = 15.0, 9.2, 2.8 Hz, 1H), 1.68 (ddd, *J* = 15.0, 10.0, 2.6 Hz, 1H), 1.36 (d, *J* = 6.4 Hz, 3H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.11 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C:202.1, 185.8, 172.5, 145.2, 128.0, 107.4, 77.5, 77.0, 76.1, 63.8, 50.3, 47.9, 45.2, 24.7, 24.4, 20.0, 11.1; IR (film) cm^{-1}: 3460, 2968, 2935, 2914, 1774, 1681, 1581, 1456, 1374, 1345, 1300, 1248, 1184, 1121, 1111, 1043, 1003, 957, 913; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{17}H_{22}NaO_6$: 345.1314, Found: 345.1309.

Synthesis of Piv Ester 16

To a solution of **12b** (1.74 g, 5.40 mmol) in pyridine (20 mL) was added PivCl (1.0 mL, 8.13 mmol) under an argon atmosphere. The reaction mixture was stirred at room temperature. After 17 hr, the reaction mixture was quenched with MeOH (3.0 mL), and the mixture was co-**evaporated with toluene. 1 M** aqueous HCl **was** added and the aqueous layer was extracted with EtOAc. Then the organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 1/1) to give **16** (2.17 g, 5.35 mmol, 99%) as a white amorphous. $[\alpha]_D^{23}$ −127.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.04 (q, *J* = 1.9 Hz, 1H), 5.30 (d, *J* = 0.8 Hz, 1H), 5.02 (t, *J* = 1.9 Hz, 1H), 5.02–4.95 (m, 1H), 4.41 (dquintet, *J* = 8.0, 6.1 Hz, 1H), 3.14 (ddd, *J* = 7.7, 1.9, 0.8 Hz, 1H), 2.79 (d, *J* = 7.7 Hz, 1H), 2.35 (dqd, *J* = 16.8, 7.3, 1.9 Hz, 1H), 2.24 (dqd, *J* = 16.8, 7.3, 1.9 Hz, 1H), 1.99 (ddd, *J* = 14.5, 8.0, 4.9 Hz, 1H), 1.96 (ddd, *J* = 14.5, 8.4, 6.1 Hz, 1H), 1.39 (d, *J* = 6.2 Hz, 3H), 1.28 (d, *J* = 6.1 Hz, 3H), 1.19 (s, 9H), 1.12 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 201.9, 185.1, 177.4, 172.0, 145.4, 127.4, 107.1, 76.7, 76.4, 76.0, 66.4, 50.1, 47.9, 42.1, 38.6, 26.9, 24.5, 20.0, 19.0, 10.9; IR (film) cm^{-1}: 3497, 2975, 2936, 2877, 1774, 1725, 1683, 1582, 1481, 1458, 1372, 1341, 1288, 1182, 1141, 1113, 1039, 914, 732; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{22}H_{30}NaO_7$: 429.1889, Found: 429.1885.

Synthesis of Lactone 18

To a solution of **16** (436 mg, 1.07 mmol) in THF (20 mL) was added BH_3·THF solution (1 M in THF, 1.5 mL, 1.50 mmol) at 0 °C under argon atmosphere, and the reaction mixture was stirred at 0 °C for

5 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/3) to give **18** (408 mg, 998 μmol, 93%) as a white amorphous. Since compound **18** was prone to decompose, it was used for the next reaction immediately after ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 5.61 (t, *J* = 1.5 Hz, 1H), 5.45 (dd, *J* = 7.0, 2.7 Hz, 1H), 5.02 (dqd, *J* = 9.9, 6.2, 3.8 Hz, 1H), 4.78 (dd, *J* = 2.6, 0.7 Hz, 1H), 4.40 (dd, *J* = 6.6, 4.2 Hz, 1H), 4.12 (dqd, *J* = 9.1, 6.2, 4.0 Hz, 1H), 3.18 (d, *J* = 6.6 Hz, 1H), 3.09 (dd, *J* = 9.3, 7.0 Hz, 1H), 3.00 (ddd, *J* = 9.3, 4.2, 0.7 Hz, 1H), 2.72 (brs, 1H), 2.32 (dqd, *J* = 9.0, 7.4, 1.7 Hz, 1H), 2.28 (dqd, *J* = 9.1, 7.1, 1.6 Hz, 1H), 1.87 (ddd, *J* = 14.7, 9.1, 3.8 Hz, 1H), 1.82 (ddd, *J* = 14.7, 9.9, 4.0 Hz, 1H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.15 (s, 9H), 1.11 (t, *J* = 7.1 Hz, 3H).

Synthesis of Enone 9

To a solution of **18** (93.5 mg, 229 μmol) in CH_2Cl_2 (3 mL) was added TFA (50 μL, 653 μmol) at 0 °C. After the reaction mixture was stirred at 0 °C for 30 min. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1) to give **9** (37.9 mg, 172 μmol, 75%) as a white crystal. $[\alpha]_D^{21}$ + 149.6 (*c* 1.18, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.77 (dd, *J* = 5.8, 2.4 Hz, 1H), 6.37 (dd, *J* = 5.8, 2.0 Hz, 1H), 6.06 (q, *J* = 2.0 Hz, 1H), 5.21 (t, *J* = 2.0 Hz, 1H), 3.86 (brs, 1H), 3.43 (dt, *J* = 7.2, 2.0 Hz, 1H), 2.74 (dd, *J* = 7.2, 2.4 Hz, 1H), 2.29 (dqd, *J* = 18.8, 7.6, 2.0 Hz, 1H), 2.24 (dqd, *J* = 18.8, 7.6, 2.0 Hz, 1H), 1.10 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 204.2, 173.9, 162.8, 145.7, 138.8, 128.4, 78.2, 77.7, 49.9, 49.1, 24.6, 11.0; IR (film) cm^{-1}: 3462, 2967, 2937, 2876, 1769, 1763, 1733, 1716, 1709, 1684, 1652, 1635, 1578, 1558, 1541, 1522, 1508, 1489, 1474, 1457, 1396, 1386, 1215, 1075, 987, 950, 895; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{12}H_{12}NaO_4$: 243.0633, Found: 243.0613.

Synthesis of Ketone 10

To a solution of **9** (948 mg, 4.31 mmol) in toluene (200 mL) under argon atmosphere was added 5% Pd/C (491 mg, 231 μmol). The atmosphere was displaced with hydrogen, and the reaction mixture was stirred at room temperature for 59 h. After filtration with Celite, the filtrate was evaporated to dryness. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 1/1) to give **10** (686 mg, 3.06 mmol, 71%) as a colorless oil and **11** (222 mg, 991 μmol, 23%) as a colorless oil. $[\alpha]_D^{22}$ + 175.4 (*c* 0.93, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.86 (t, *J* = 1.2 Hz, 1H), 3.50 (brs, 1H), 2.93 (ddd, *J* = 10.8, 8.4, 4.8 Hz, 1H), 2.63 (dt, *J* = 10.8, 1.2 Hz, 1H), 2.38–2.14 (m, 4H), 1.94–1.80 (m, 2H), 1.55 (dquintet, *J* = 14.4, 7.2 Hz, 1H), 1.45 (dd, *J* = 13.4, 3.8 Hz, 1H), 1.41 (dquintet, *J* = 14.4, 7.2 Hz, 1H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 216.0, 176.8, 78.4, 72.6, 50.8, 41.7, 39.4, 37.6, 37.2, 26.5, 21.8, 11.2; IR (film) cm^{-1}: 3445, 2962, 2935, 2874, 1742, 1457, 1274, 1123, 1007, 959; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{12}H_{16}NaO_4$: 247.0946, Found: 247.0936.

Synthesis of Methyl Ester 24

To a solution of **10** (64.3 mg, 287 μmol) in MeOH (3 mL) was added NaOMe (64.0 mg, 1.18 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred for 30 min, the reaction mixture was quenched with **0.5 M** aqueous HCl. The mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, to a solution of the residue in MeOH (21 mL) was added 10% Pd/C (110 mg, 150 μmol) under argon atmosphere. The atmosphere was displaced with hydrogen, and then the reaction mixture was stirred at room temperature for 11 h. After filtration through Celite, the filtrate was evaporated. The residue was carried on to the next step without further purification due to its adequate purity and high polarity. To a solution of the residue in MeOH (2.5 mL) and benzene (2.5 mL) was added TMS diazomethane solution (0.6 M in *n*-hexane, 1.2 mL, 0.72 mmol) at 0 °C for 10 min. The reaction mixture was concentrated under reduced pressure to afford *cis*-**23** (70.1 mg). The crude product was used for the next reaction without further purification. To a solution of *cis*-**23** in pyridine (3 mL) was added phosphorus oxychloride (0.4 ml, 4.29 mmol) at 0 °C under argon atmosphere. The reaction mixture was gradually warmed to room temperature with overnight stirring. The reaction mixture was quenched with slow addition of cold H_2O, and then extracted with Et_2O. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/AcOEt = 4/1) to give **24** (30.1 mg, 0.14 mmol, 47% in 4 steps) as a colorless oil. All spectral data of **24** were identical to those reported.[25]

Synthesis of CFA (4)

A suspension of **24** (130 mg, 583 μmol) in 3 M aqueous HCl (8.0 mL) was refluxed for 6 h. After the reaction mixture was quenched with H_2O, the mixture was extracted with EtOAc. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, coronafacic acid **4** (122 mg, 583 μmol, quant.) was obtained as a colorless crystalline solid. All spectral data of **4** were identical to those reported.[25]

Synthesis of Chiral Acetal *ent*-8

To a solution of 4-cyclopentene-1,3-dione (2.30 g, 24.0 mmol) and (2*S*,4*S*)-(+)-2,4-pentanediol (1.95 g, 18.7 mmol) in toluene (120 mL) was added $TsOH{\cdot}H_2O$ (351 mg, 1.85 mmol) and the reaction mixture was stirred and refluxed for 1 h. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1) to give *ent*-**8** (2.52 g, 13.8 mmol, 74%) as a colorless oil. $[\alpha]_D^{24}$ −16.4 (*c* 1.14, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.46 (d, *J* = 5.8 Hz, 1H), 6.19 (d, *J* = 5.8 Hz, 1H), 4.17 (dquintet, *J* = 7.8, 6.1 Hz, 1H), 4.06 (dquintet, *J* = 8.2, 6.1 Hz, 1H), 2.68 (d, *J* = 17.9 Hz, 1H), 2.58 (d, *J* = 17.9 Hz, 1H), 1.75 (ddd, *J* = 13.2, 8.2, 6.1 Hz, 1H), 1.71 (ddd, *J* = 13.2, 7.8, 6.1 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H), 1.26 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 204.9, 157.5, 134.8, 105.0, 65.4, 65.2, 47.3, 39.7, 21.8, 21.4; IR (film) cm^{-1}: 2974, 2927, 2878, 1737, 1463, 1379, 1346, 1276, 1161, 1022, 798; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{10}H_{14}NaO_3$: 205.0841, Found: 205.0840.

Synthesis of Diels-Alder Type Reaction Product *ent*-12b

To a solution of **7** (1.46 g, 10.4 mmol) and *ent*-**8** (2.71 g, 14.9 mmol) in CH_2Cl_2 (70 mL) was added Et_3N (1.5 mL, 10.7 mmol) at −40 °C under argon atmosphere. The reaction mixture was stirred at −40 °C for 1 d. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/3) to give *ent*-**12b** (1.99 g, 6.17 mmol, 59%) as a white crystal and the diastereomer *ent*-**13b** (575 mg, 0.78 mmol, 17%) as a white crystal. *ent*-**12b**: $[\alpha]_D^{20}$ + 176.9 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.07 (q, *J* = 1.9 Hz, 1H), 5.43 (d, *J* = 0.7 Hz, 1H), 5.05 (t, *J* = 1.9 Hz, 1H), 4.67 (dqd, *J* = 9.4, 6.2, 2.9 Hz, 1H), 4.13 (brs, 1H), 3.94 (dqd, *J* = 9.9, 6.3, 2.8 Hz, 1H), 3.19 (ddd, *J* = 7.6, 1.9, 0.7 Hz, 1H), 2.79 (d, *J* = 7.6 Hz, 1H), 2.31 (dqd, *J* = 17.6, 7.3, 1.9 Hz, 1H), 2.25 (dqd, *J* = 17.6, 7.3, 1.9 Hz, 1H), 1.86 (ddd, *J* = 14.7, 9.4, 2.8 Hz, 1H), 1.69 (ddd, *J* = 14.7, 9.9,

2.9 Hz, 1H), 1.38 (d, J=6.2 Hz, 3H), 1.24 (d, J=6.3 Hz, 3H), 1.12 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 202.1, 185.9, 172.8, 145.2, 128.2, 107.4, 77.9, 77.1, 76.4, 63.5, 50.4, 48.2, 45.4, 24.8, 24.5, 20.0, 11.2; IR (film) cm^{-1}: 3390, 2972, 2933, 2878, 1771, 1677, 1578, 1458, 1372, 1340, 1186, 1114, 957, 911; HRMS (ESI, positive) *m/z* [M+Na]$^+$ Calcd. for $C_{17}H_{22}NaO_6$: 345.1314, Found: 345.1313. *ent*-**13b**: $[\alpha]_D^{22}$−75.1 (*c* 1.11, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.06 (q, J=2.0 Hz, 1H), 5.41 (d, J=0.8 Hz, 1H), 5.04 (t, J=2.0 Hz, 1H), 4.65 (dqd, J=9.2, 6.4, 2.8 Hz, 1H), 3.93 (dqd, J=10.0, 6.0, 3.2 Hz, 1H), 3.18 (ddd, J= 7.2, 2.0, 0.8 Hz, 1H), 2.79 (d, J=7.2 Hz, 1H), 2.32 (dqd, J=16.4, 7.2, 2.0 Hz, 1H), 2.26 (dqd, J=16.4, 7.2, 2.0 Hz, 1H), 1.88 (ddd, J=14.8, 9.2, 2.8 Hz, 1H), 1.69 (ddd, J=14.8, 10.0, 3.2 Hz, 1H), 1.36 (d, J=6.4 Hz, 3H), 1.26 (d, J=6.0 Hz, 3H), 1.11 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 202.1, 185.8, 172.5, 145.2, 128.0, 107.5, 77.5, 77.0, 76.1, 63.9, 50.3, 47.9, 45.2, 24.7, 24.4, 19.5, 11.1; IR (film) cm^{-1}: 3468, 2971, 2933, 2882, 1771, 1680, 1579, 1457, 1375, 1339, 1250, 1184, 1039, 999, 912, 861, 760; HRMS (ESI, positive) *m/z* [M+Na]$^+$ Calcd. for $C_{17}H_{22}NaO_6$: 345.1314, Found: 345.1303.

Synthesis of Piv Ester *ent*-16

To a solution of *ent*-**12b** (1.68 g, 5.21 mmol) in pyridine (20 mL) was added PivCl (970 μL, 7.89 mmol) under argon atmosphere and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was quenched with MeOH (3.0 mL), and the mixture was co-**evaporated with toluene. 1 M** aqueous HCl **was** added and the aqueous layer was extracted with EtOAc. Then the organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/acetone=30/1–20/1) to give *ent*-**16** (2.10 g, 5.16 mmol, 99%) as a white crystal. $[\alpha]_D^{20}$+123.9 (*c* 1.06, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.04 (q, J=1.9 Hz, 1H), 5.30 (d, J=0.8 Hz, 1H), 5.02 (t, J=1.9 Hz, 1H), 5.02–4.95 (m, 1H), 4.41 (dquintet, J=8.0, 6.1 Hz, 1H), 3.14 (ddd, J=7.7, 1.9, 0.8 Hz, 1H), 2.79 (d, 7.7 Hz, 1H), 2.35 (dqd, J=16.8, 7.3, 1.9 Hz, 1H), 2.24 (dqd, J=16.8, 7.3, 1.9 Hz, 1H), 1.99 (ddd, J=14.5, 8.0, 4.9 Hz, 1H), 1.96 (ddd, J=14.5, 8.4, 6.1 Hz, 1H), 1.39 (d, J=6.2 Hz, 3H), 1.28 (d, J=6.1 Hz, 3H), 1.19 (s, 9H), 1.12 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 201.9, 185.1, 177.4, 172.0, 145.4, 127.4, 107.1, 76.7, 76.4, 76.0, 66.4, 50.1, 47.9, 42.1, 38.6, 26.9, 24.5, 20.0, 19.0, 10.9; IR (film) cm^{-1}: 3493, 2975, 2937, 2876, 1773, 1725, 1683, 1583, 1481, 1458, 1378, 1341, 1328, 1288, 1181, 1142, 1114, 1038, 913, 732; HRMS (ESI, positive) *m/z* [M+Na]$^+$ Calcd. for $C_{22}H_{30}NaO_7$: 429.1889, Found: 429.1889.

Synthesis of Lactone *ent*-18

To a solution of *ent*-**16** (2.10 g, 5.17 mmol) in THF (95 mL) was added BH_3·THF solution (1 M in THF, 6.7 mL, 6.70 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred at 0 °C for 6 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. **1 M** aqueous HCl **was** added and the aqueous layer was extracted with EtOAc. Then the organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/acetone=30/1–20/1) to give *ent*-**18** (1.75 g, 4.28 mmol, 83%) as a white amorphous. Since compound *ent*-**18** was easily decomposed, it was used for the next reaction immediately after ^{1}H NMR analysis. ^{1}H NMR δ_H ($CDCl_3$) 5.61 (t, J=1.5 Hz, 1H), 5.45 (dd, J=7.0, 2.7 Hz, 1H), 5.02 (dqd, J=9.9, 6.2, 3.8 Hz, 1H), 4.78 (dd, J=2.6, 0.7 Hz, 1H), 4.40 (dd, J=6.6, 4.2 Hz, 1H), 4.12 (dqd, J=9.1, 6.2, 4.0 Hz, 1H), 3.18 (d, J=6.6 Hz, 1H), 3.09 (dd, J=9.3, 7.0 Hz, 1H), 3.00 (ddd, J=9.3, 4.2, 0.7 Hz, 1H), 2.72 (brs, 1H), 2.32 (dqd, J=9.0, 7.4, 1.7 Hz, 1H), 2.28 (dqd, J=9.1, 7.1, 1.6 Hz, 1H), 1.87 (ddd, J=14.7, 9.1, 3.8 Hz, 1H), 1.82 (ddd, J=14.7, 9.9, 4.0 Hz, 1H), 1.29 (d, J=6.2 Hz, 3H), 1.22 (d, J=6.2 Hz, 3H), 1.15 (s, 9H), 1.11 (t, J=7.1 Hz, 3H).

Synthesis of Enone *ent*-9

To a solution of *ent*-**18** (22.0 mg, 53.9 μmol) in CH_2Cl_2 (3 mL) was added TFA (2 μL, 261 μmol) at 0 °C. After the reaction mixture was stirred at 0 °C for 1 h. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc=2/3) to give *ent*-**9** (5.4 mg, 24.1 μmol, 45%) as a white crystal. $[\alpha]_D^{21}$−155.3 (*c* 1.39, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.75 (dd, J=5.8, 2.6 Hz, 1H), 6.37 (dd, J=5.8, 2.0 Hz, 1H), 6.06 (q, J=2.0 Hz, 1H), 5.21 (t, J=2.0 Hz, 1H), 3.65 (brs, 1H), 3.43 (dt, J=6.8, 2.0 Hz, 1H), 2.73 (dd, J=6.8, 2.6 Hz, 1H), 2.29 (dqd, J=17.2, 7.6, 2.0 Hz, 1H), 2.24 (dqd, 17.2, 7.6, 2.0 Hz, 1H), 1.10 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 204.0, 174.0, 162.8, 145.8, 138.8, 128.4, 78.2, 77.7, 49.8, 49.1, 24.6, 11.0; IR (film) cm^{-1}: 3443, 2971, 2938, 2879, 1770, 1760, 1749, 1733, 1716, 1705, 1684, 1671, 1646, 1578, 1520, 1487, 1420, 1339, 1211, 1074, 999, 930, 893; HRMS (ESI, positive) *m/z* [M+Na]$^+$ Calcd. for $C_{12}H_{12}NaO_4$: 243.0633. Found: 243.0613.

Synthesis of ketone *ent*-10

To a solution of *ent*-**9** (391 mg, 1.78 mmol) in toluene (90 mL) under argon atmosphere was added 5% Pd/C (37.6 mg, 17.7 μmol). The atmosphere was displaced with hydrogen, and the reaction mixture was stirred at room temperature for 48 h. After filtration with Celite, the filtrate was evaporated to dryness. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc=1/1) to give *ent*-**10** (269 mg, 1.20 mmol, 68%) as a colorless oil and *ent*-**11** (94.8 mg, 423 μmol, 22%) as a colorless oil. $[\alpha]_D^{20}$−168.0 (*c* 0.74, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.85 (t, J=1.2 Hz, 1H), 3.50 (brs, 1H), 2.93 (ddd, J=10.4, 9.2, 6.0 Hz, 1H), 2.63 (dt, J=10.4, 1.2 Hz, 1H), 2.38–2.12 (m, 4H), 1.94–1.80 (m, 2H), 1.55 (dquintet, J=14.8, 7.2 Hz, 1H), 1.44 (dd, J=13.6, 4.4 Hz, 1H), 1.40 (dquintet, J=14.8, 7.2 Hz, 1H), 0.95 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 216.0, 176.9, 78.4, 72.6, 50.9, 41.7, 39.4, 37.6, 37.2, 26.5, 21.8, 11.2; IR (film) cm^{-1}: 3452, 2965, 2932, 2874, 1745, 1459, 1260, 1124, 1010, 960; HRMS (ESI, positive) *m/z* [M+Na]$^+$ Calcd. for $C_{12}H_{16}NaO_4$: 247.0946, Found: 247.0985.

Synthesis of Methyl Ester *ent*-24

To a solution of *ent*-**10** (202 mg, 901 μmol) in MeOH (9 mL) was added NaOMe (69.3 mg, 1.28 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred for 30 min, the reaction mixture was quenched with 0.5 M aqueous HCl. The mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, to a solution of the residue in MeOH (10 mL) was added 10% Pd/C (49.2 mg, 461 μmol) under argon atmosphere. The atmosphere was displaced with hydrogen, and then the reaction mixture was stirred at room temperature for 40 min. After filtration with Celite, the filtrate was evaporated. The residue was carried on to the next step without further purification because this compound was pure enough and highly polar. To a solution of the residue in MeOH (6 mL) and benzene (6 mL) was added TMS diazomethane solution (0.6 M in *n*-hexane, 1.5 mL, 900 μmol) at 0 °C for 10 min. The reaction mixture was concentrated under reduced pressure to afford *ent-cis*-**23** (461 mg). The crude product was used for the next reaction without further purification. To a solution of *ent-cis*-**23** in pyridine (8 mL) was added phosphorus oxychloride (1.6 mL, 17.1 mmol) at 0 °C under argon atmosphere.

The reaction mixture was stirred at room temperature for 11 h. The reaction mixture was quenched with slow addition of cold H_2O, and then extracted with Et_2O. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/acetone = 4/1) to give *ent*-**24** (132 mg, 595 μmol, 66% in 4 steps) as a colorless oil. All spectral data of *ent*-**24** were identical to those reported. [25]

Synthesis of *ent*-CFA (*ent*-4)

A suspension of *ent*-**24** (94.9 mg, 427 μmol) in 3 M aqueous HCl (5.0 mL) was refluxed for 6 h. After the reaction mixture was quenched with H_2O, the mixture was extracted with EtOAc. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, coronafacic acid *ent*-**4** (87.8 mg, 423 μmol, 99%) was obtained as a colorless crystalline solid. All spectral data of *ent*-**4** were identical to those reported.[25]

Synthesis of Ketone 11

To a solution of **9** (453 mg, 2.06 mmol) in CH_2Cl_2 (20 mL) was added Crabtree's catalyst (100 mg, 124 μmol) under argon atmosphere. The atmosphere was displaced with hydrogen, and the reaction mixture was stirred at room temperature for 5 days. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1) to give **11** (352 mg, 1.57 mmol, 76%) as a colorless oil and **10** (76.2 mg, 340 μmol, 16%) as a colorless oil. $[\alpha]_D^{24}$ + 156.5 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.79 (dd, *J* = 3.1, 1.9 Hz, 1H), 3.43 (brs, 1H), 2.87 (ddd, *J* = 10.8, 8.9, 5.7 Hz, 1H), 2.74 (dt, *J* = 10.8, 1.2 Hz, 1H), 2.36–2.15 (m, 4H), 2.08 (dd, *J* = 12.8, 10.8 Hz, 1H), 1.87–1.78 (m, 1H), 1.58 (dd, *J* = 12.8, 6.6 Hz, 1H), 1.45 (dsext, *J* = 14.9, 7.5 Hz, 1H), 1.32 (dsext, *J* = 14.9, 7.5 Hz, 1H), 0.99 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 217.2, 176.9, 79.3, 72.9, 46.7, 42.4, 39.5, 37.4, 37.3, 26.4, 22.0, 11.7; IR (film) cm^{-1}: 3457, 2964, 2933, 2872, 1742, 1458, 1261, 1128, 1009, 968; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{12}H_{16}NaO_4$: 247.0946. Found: 247.0943.

Synthesis of Methyl Ester 30

To a solution of **11** (79.8 mg, 356 μmol) in MeOH (4 mL) was added NaOMe (54.3 mg, 1.81 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred for 1 h, the reaction mixture was quenched with 1 M aqueous HCl. The mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, to a solution of the residue in MeOH (4.0 mL) and benzene (4.0 mL) was added TMS diazomethane solution (0.6 M in *n*-hexane, 2.0 mL, 1.2 mmol) at 0 °C. The reaction mixture was quenched with acetic acid (2 mL) and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 3/2) to give **30** (73.0 mg, 306 μmol, 86%) as a white crystal. $[\alpha]_D^{22}$ + 73.7 (*c* 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.67 (dd, *J* = 3.8, 3.0, 1H), 3.73 (s, 3H), 3.66 (s, 1H), 2.93 (ddd, *J* = 14.8, 7.1, 3.8 Hz, 1H), 2.53 (tddd, *J* = 10.7, 7.0, 6.0, 4.4, 3.0 Hz, 1H), 2.45–2.21 (m, 3H), 2.09 (dd, 13.8, 6.0 Hz), 1.63 (dd, *J* = 13.8, 10.7 Hz, 1H), 1.55 (dquintet, *J* = 14.2, 7.0 Hz, 1H), 1.47 (dquintet, *J* = 14.2, 7.0 Hz, 1H), 1.34–1.20 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 205.4, 175.4, 136.7, 135.8, 76.4, 53.0, 47.4, 40.7, 38.9, 38.4, 27.8, 22.8, 11.5; IR (film) cm^{-1}: 3456, 2962, 2870, 1724, 1655, 1454, 1219, 1107; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{13}H_{18}NaO_4$: 261.1097, Found: 261.1132.

Synthesis of Dehydration Reaction Precursor of *cis*-27

To a solution of **30** (29.7 mg, 125 μmol) in MeOH (5 mL) was added 5% Pd/C (14.0 mg, 6.5 μmol) under argon atmosphere. The atmosphere was displaced with hydrogen, and then the reaction mixture was stirred for 2 h at rt. After filtration with Celite, the filtrate was evaporated and purified by silica gel column chromatography (*n*-hexane/EtOAc = 3/2) to give *cis*-**27** (26.3 mg, 110 μmol, 88%) as a colorless oil. $[\alpha]_D^{22}$ + 82.7 (*c* 0.95, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.72 (s, 3H), 3.38 (s, 1H), 3.57–2.44 (m, 2H), 2.30-1.96 (m, 4H), 1.96–1.80 (m, 2H), 1.65 (ddddd, *J* = 10.8, 10.5, 6.7, 3.8 3.7 Hz, 1H), 1.38–1.18 (m, 4H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{1}H NMR (400 MHz, pyridine-d_5) δ_H: 3.68 (s, 3H), 2.81 (td, *J* = 8.4, 6.0 Hz, 1H), 2.68 (ddd, *J* = 7.6, 6.0, 4.6 Hz, 1H), 2.37–2.14 (m, 4H), 2.30–1.96 (m, 4H), 2.10–1.95 (m, 2H), 1.82–1.70 (m, 1H), 1.63 (dd, *J* = 13.5, 9.0 Hz, 1H), 1.47–1.30 (m, 3H), 0.83 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 217.6, 176.1, 76.4, 52.3, 47.9, 44.9, 40.2, 35.3, 32.4, 29.1, 26.5, 21.4, 11.7; IR (film) cm^{-1}: 3471, 2954, 2870, 1736, 1454, 1246; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{13}H_{20}NaO_4$: 263.1254, Found: 263.1249.

Synthesis of α,β-Unsaturated ester 28

To a solution of *cis*-**27** (62.1 mg, 259 μmol) in pyridine (2.8 mL) was added phosphorus oxychloride (280 μL, 3.1 mmol) at 0 °C under argon atmosphere. The reaction mixture was gradually warmed to room temperature with overnight stirring. The reaction mixture was quenched with slow addition of cold H_2O, and then extracted with Et_2O. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel short pass to give the mixture of **28** and **29** (8:1, 50.6 mg, 87%) as a colorless oil. The mixture was separated by silica gel column chromatography (*n*-hexane/EtOAc = 9/1). **28**: $[\alpha]_D^{22}$ + 157.7 (*c* 1.08, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.98 (d, *J* = 2.2 Hz, 1H), 3.77 (s, 3H), 3.32-3.23 (m, 1H), 2.49 (tdd, *J* = 7.5, 4.4, 1.0 Hz, 1H), 2.33–2.09 (m, 3H), 2.08–1.89 (m, 3H), 1.48–1.31 (m, 3H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 221.4, 167.6, 145.5, 131.2, 51.9, 46.1, 37.0, 36.1, 34.9, 27.9, 27.2, 25.7, 11.7; IR (film) cm^{-1}: 2954, 2877, 1716, 1643, 1442, 1257, 1146, 1080, 756; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{13}H_{18}NaO_3$: 245.1148, Found: 245.1168.

29: ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 3.68 (s, 3H), 2.72 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.66 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.41–2.15 (m, 5H), 2.10–1.97 (m, 1H), 1.41 (dd, *J* = 13.6, 7.9 Hz, 1H), 1.31 (q, *J* = 6.8 Hz, 1H), 1.27–1.17 (m, 2H), 0.84 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$) δ_C 212.7, 171.2, 55.3, 52.3, 49.0, 47.3, 45.1, 40.6, 37.0, 32.9, 29.2, 20.1, 12.9. ESI-MS *m/z* 245 $(M+Na)^+$.

Synthesis of 6-*epi*-CFA (6)

A suspension of **28** (34.9 mg, 15.6 μmol) in 3 M aqueous HCl (840 μL) was refluxed for 6.5 h. After the reaction mixture was quenched with H_2O, the mixture was extracted with EtOAc. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, 6-*epi*-CFA (**6**) (32.3 mg, 15.5 μmol, quant.) was obtained as a colorless crystalline solid. $[\alpha]_D^{23}$ + 133.9 (*c* 0.575, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.15 (dd, *J* = 3.1, 1.0 Hz, 1H), 3.27 (ddt, *J* = 12.4, 6.6, 1.7, 1H), 2.51 (ddd, *J* = 12.4, 6.2, 1.3 Hz, 1H), 2.30 (td, *J* = 11.3, 7.0 Hz, 1H), 2.79 (d, *J* = 7.5 Hz, 1H), 2.32 (dqd, *J* = 16.4, 7.3, 1.9 Hz, 1H), 2.26 (dqd, *J* = 16.4, 7.3, 1.9 Hz, 1H), 2.04 (qd, *J* = 7.5, 5.8 Hz, 1H), 2.03 (ddd, *J* = 12.4, 6.6, 5.5 Hz, 1H), 1.46 (dquint., *J* = 14.6, 7.4 Hz, 1H), 1.43–1.41 (m, 1H), 1.38 (dquint., *J* = 14.6, 7.4 Hz, 1H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 221.2, 172.3, 148.2, 130.6, 45.9, 36.9, 35.8, 35.1, 27.7, 27.1, 25.5, 11.6; IR (film) cm^{-1}: 3039, 2962, 2933, 2876, 1739,

1685, 1636, 1461, 1406, 1275, 1233, 1146, 1054, 929, 890; HRMS (ESI, negative) *m/z* $[M-H]^-$ Calcd. for $C_{12}H_{16}NaO_3$: 231.0992, Found: 231.0993.

Synthesis of Ketone *ent*-11

To a solution of *ent*-**9** (395 mg, 1,79 mmol) in CH_2Cl_2 (15 mL) was added Crabtree's catalyst (100 mg, 124 μmol). The atmosphere was displaced with hydrogen, and the reaction mixture was stirred at room temperature for 5 days. After evaporation, the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 4/6) to give *ent*-**11** (299 mg, 1.33 mmol, 74%) as a colorless oil and *ent*-**10** (97.1 mg, 433 μmol, 25%) as a colorless oil. $[\alpha]_D^{24}$ −155.8 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ_H: 4.79 (dd, *J* = 2.8, 1.2 Hz, 1H), 3.43 (brs, 1H), 2.88 (ddd, *J* = 10.8, 9.2, 6.4 Hz, 1H), 2.76 (dt, *J* = 10.8, 1.2 Hz, 1H), 2.36–2.15 (m, 4H), 2.09 (dd, *J* = 12.8, 10.4 Hz, 1H), 1.87–1.78 (m, 1H), 1.57 (dd, *J* = 12.8, 6.4 Hz, 1H), 1.45 (dquintet, *J* = 14.8, 7.6 Hz, 1H), 1.33 (dquintet, *J* = 14.8, 7.6 Hz, 1H), 0.98 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 217.2, 176.9, 79.3, 72.9, 46.7, 42.4, 39.5, 37.4, 37.3, 26.4, 22.0, 11.7; IR (film) cm^{-1}: 3457, 2964, 2936, 2878, 1744, 1458, 1265, 1132, 968 (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{12}H_{16}NaO_4$: 247.0946, Found: 247.0934.

Synthesis of Methyl Ester *ent*-30

To a solution of *ent*-**11** (54.6 mg, 244 μmol) in MeOH (3 mL) was added NaOMe (54.3 mg, 1.0 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred for 1 h, the reaction mixture was quenched with 1 M aqueous HCl. The mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, to a solution of the residue in MeOH (3.0 mL) and benzene (3.0 mL) was added TMS diazomethane solution (0.6 M in *n*-hexane, 1.5 mL, 0.9 mmol) at 0 °C. The reaction mixture was quenched with acetic acid (2 mL) and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 3/2) to give *ent*-**30** (52.9 mg, 222 μmol, 91%) as a white crystal. $[\alpha]_D^{22}$ −76.6 (*c* 1.04, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ_H: 6.67 (dd, *J* = 3.8, 3.0, 1H), 3.73 (s, 3H), 3.66 (s, 1H), 2.93 (ddd, *J* = 14.8, 7.1, 3.8 Hz, 1H), 2.53 (tddd, *J* = 10.7, 7.0, 6.0, 4.4, 3.0 Hz, 1H), 2.45-2.21 (m, 3H), 2.09 (dd, 13.8, 6.0 Hz), 1.63 (dd, *J* = 13.8, 10.7 Hz, 1H), 1.55 (dquintet, *J* = 14.2, 7.0 Hz, 1H), 1.47 (dquintet, *J* = 14.2, 7.0 Hz, 1H), 1.34–1.20 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 205.4, 175.4, 136.7, 135.8, 76.4, 53.0, 47.4, 40.7, 38.9, 38.4, 27.8, 22.8, 11.5; IR (film) cm^{-1}: 3456, 2962, 2870, 1720, 1655, 1455, 1219, 1107; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{13}H_{18}NaO_4$: 261.1097, Found: 261.1121.

Synthesis of Dehydration Reaction Precursor of *ent-cis*-27

To a solution of *ent*-**30** (35.7 mg, 150 μmol) in MeOH (6 mL) was added 5% Pd/C (15.0 mg, 7.0 μmol) under argon atmosphere. The atmosphere was displaced with hydrogen, and then the reaction mixture was stirred for 2 h at rt. After filtration with Celite, the filtrate was evaporated and purified by silica gel column chromatography (*n*-hexane/EtOAc = 3/2) to give *ent-cis*-**27** (35.1 mg, 146 μmol, 98%) as a colorless oil. $[\alpha]_D^{22}$ −79.6 (*c* 1.09, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ_H: 3.72 (s, 3H), 3.38 (s, 1H), 3.57–2.44 (m, 2H), 2.30-1.96 (m, 4H), 1.96–1.80 (m, 2H), 1.65 (ddddd, *J* = 10.8, 10.5, 6.7, 3.8 3.7 Hz, 1H), 1.38-1.18 (m, 4H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 217.6, 176.2, 76.4, 52.3, 47.9, 44.9, 40.2, 35.3, 32.4, 29.1, 26.6, 21.5, 11.7; IR (film) cm^{-1}: 3475, 2954, 2870, 1736, 1454, 1246; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{13}H_{20}NaO_4$: 263.1254, Found: 263.1262.

Synthesis of α,β-Unsaturated Ester *ent*-28

To a solution of *ent-cis*-**27** (124.3 mg, 108 μmol) in pyridine (5.7 mL) was added phosphorus oxychloride (480 μL, 5.17 mmol) at 0 °C under argon atmosphere. The reaction mixture was gradually warmed to room temperature with overnight stirring. The reaction mixture was quenched with slow addition of cold H_2O, and then extracted with Et_2O. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, the residue was purified by silica gel short pass to give the mixture of *ent*-**28** and *ent*-**29** (6.3:1, 101.0 mg, 87%) as a colorless oil. The mixture was separated by silica gel column chromatography (*n*-hexane/EtOAc = 9/1). *ent*-**28**: $[\alpha]_D^{22}$ −160.5 (*c* 1.08, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ_H: 6.98 (d, *J* = 2.2 Hz, 1H), 3.77 (s, 3H), 3.32–3.23 (m, 1H), 2.49 (tdd, *J* = 7.5, 4.4, 1.0 Hz, 1H), 2.33–2.09 (m, 3H), 2.08–1.89 (m, 3H), 1.48–1.31 (m, 3H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 221.4, 167.6, 145.5, 131.2, 51.9, 46.1, 37.0, 36.1, 34.9, 27.9, 27.2, 25.7, 11.7; IR (film) cm^{-1}: 2958, 2877, 1716, 1643, 1442, 1257, 1146, 1080, 756; HRMS (ESI, positive) *m/z* $[M+Na]^+$ Calcd. for $C_{13}H_{18}NaO_3$: 245.1148, Found: 245.1165.

Synthesis of *ent*-6-*epi*-CFA (*ent*-6)

A suspension of *ent*-**28** (125 mg, 559 μmol) in 3 M aqueous HCl (8 ml) was refluxed for 6 h. After the reaction mixture was quenched with H_2O, the mixture was extracted with EtOAc. The resulting organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4, and filtered. After evaporation, *ent*-6-*epi*-CFA (*ent*-**6**) (122 mg, 586 μmol, quant.) was obtained as a colorless crystalline solid. $[\alpha]_D^{22}$ −126.8 (*c* 0.69, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.15 (dd, *J* = 3.2, 1.2 Hz, 1H), 3.27 (ddt, *J* = 12.4, 6.6, 1.6, 1H), 2.51 (ddd, *J* = 12.4, 6.4, 1.4 Hz, 1H), 2.31 (td, *J* = 11.2, 7.0 Hz, 1H), 2.79 (d, *J* = 7.6 Hz, 1H), 2.32 (dqd, *J* = 16.4, 7.4, 2.0 Hz, 1H), 2.26 (dqd, *J* = 16.4, 7.4, 2.0 Hz, 1H), 2.04 (qd, *J* = 7.6, 5.8 Hz, 1H), 2.03 (ddd, *J* = 12.4, 6.6, 5.6 Hz, 1H), 1.46 (dquint., *J* = 14.6, 7.4 Hz, 1H), 1.43–1.41 (m, 1H), 1.37 (dquint., *J* = 15.2, 7.6 Hz, 1H), 0.98 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 221.0, 171.8, 148.1, 130.3, 45.7, 36.8, 35.7, 34.9, 27.5, 26.9, 25.3, 11.4; IR (film) cm^{-1}: 2963, 2933, 2878, 1741, 1684, 1634, 1458, 1418, 1274, 1220, 1147, 1051, 924, 887; HRMS (ESI, negative) *m/z* $[M-H]^-$ Calcd. for $C_{12}H_{15}O_3$: 207.1027, Found: 207.1054.

Chiral HPLC analysis

Coronafacic Acid Methyl Ester 24 and ent-*24*

Optical purities were determined by chiral HPLC analyses on a Chiralpak IA Φ4.6 × 250 mm column (Daicel Co., Ltd., Japan) eluting with 99% *n*-hexane containing 1% EtOH at 0.5 mL/min. Under these conditions, good separation of each enantiomer was achieved: coronafacic acid methyl ester **24** at Rt = 28.3 min and *ent*-**24** at Rt 27.7 min. Enantiomeric excess was calculated from the ratio of peak areas (mAu s) at 235 nm. Chiral HPLC analysis of 25 ng of the synthetic **24** gave a ratio of **24**: *ent*-**24** = 9789214: 22582, which corresponded to > 99.5% ee. According to the above-mentioned procedure, Chiral HPLC analysis of 45 ng of the synthetic *ent*-**24** gave a ratio of **24**: *ent*-**24** = 29444: 14203903, which corresponded to > 99.5% ee.

C6-epi-*Coronafacic Acid Methyl Ester 28 and* ent-*28*

Optical purities were determined by chiral HPLC analyses on a Chiralpak IA Φ4.6 × 250 mm column (Daicel Co., Ltd., Japan) eluting with 98% *n*-hexane containing 2% *i*PrOH at 1.0 mL/min. Under these conditions, good separation of each enantiomer was

achieved: C6-*epi*-coronafacic acid methyl ester **28** at Rt = 9.0 min and *ent*-**28** at Rt 9.8 min. Enantiomeric excess was calculated from the ratio of peak areas (mAu s) at 235 nm. Chiral HPLC analysis of 10 ng of the synthetic **28** gave a ratio of **28**: *ent*-**28** = 2320104: 2954, which corresponded to > 99% ee. According to the above-mentioned procedure, Chiral HPLC analysis of 15 ng of the synthetic *ent*-**28** gave a ratio of **28**: *ent*-**28** = 47987: 3347993, which corresponded to 97.2% ee.

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Conflict of Interest

The authors declare no conflict of interest.

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[1] C. Wasternack, *Ann. Bot.* **2007**, *100*, 681–697.
[2] C. Wasternack, B. Hause, *Ann. Bot.* **2013**, *111*, 1021–1058.
[3] C. Wasternack, *J. Plant Growth Regul.* **2015**, *34*, 761–794.
[4] S. Fonseca, A. Chini, M. Hamberg, B. Adie, A. Porzel, R. Kramell, O. Miersch, C. Wasternack, R. Solano, *Nature Chem.Biol.* **2009**, *5*, 344–350.
[5] A. Ichihara, K. Shiraishi, H. Sato, S. Sakamura, K. Nishiyama, R. Sakai, A. Furusaki, T. Matsumoto, *J. Am. Chem. Soc.* **1977**, *99*, 636–637.
[6] E. W. Weiler, T. M. Kutchan, T. Gorba, W. Brodschelm, U. Niesel, F. Bublitz, *FEBS Lett.* **1994**, *345*, 9–13.
[7] Y. Takaoka, M. Iwahashi, A. Chini, H. Saito, Y. Ishimaru, S. Egoshi, N. Kato, M. Tanaka, K. Bashir, M. Seki, R. Solano, M. Ueda, *Nat. Commun.* **2018**, *9*, 3654.
[8] M. Ueda, T. Kaji, W. Kozaki, *Int. J. Mol. Sci.* **2020**, *21*, 1124.
[9] A. Gaucher, J. Ollivier, J. Marguerite, R. Paugam, J. Salaün, *Can. J. Chem.* **1994**, *72*, 1312–1327.
[10] A. B. Charette, B. Cote, *J. Am. Chem. Soc.* **1995**, *117*, 12721–12732.
[11] H. Toshima, A. Ichihara, *Biosci. Biotechnol. Biochem.* **1995**, *59*, 497–500.
[12] CFA has four stable stereoisomers. The stereochemistries at C7a of *trans*-stereoisomers, which have a *trans* ring junction, are readily epimerised to give *cis* stereoisomers.[13]
[13] M. M. Littleson, C. J. Russell, E. E. Frye, K. B. Ling, C. Jamieson, A. J. B. Watson, *Synthesis* **2016**, *48*, 3429–3448, and references cited therein.
[14] M. M. Littleson, C. M. Baker, A. J. Dalencon, E. C. Frye, C. Jamieson, A. R. Kennedy, K. B. Ling, M. M. McLachlan, M. G. Montgomery, C. J. Russell, A. J. B. Watson, *Nat. Commun.* **2018**, *9*, 1105.
[15] N. Kato, S. Miyagawa, H. Nomoto, M. Nakayama, M. Iwashita, M. Ueda, *Chirality* **2020**, *32*, in press.
[16] a) M. Okada, S. Ito, A. Matsubara, I. Iwakura, S. Egoshi, M. Ueda, *Org. Biomol. Chem.* **2009**, *7*, 3065–3073; b) M. Okada, S. Egoshi, M. Ueda, *Biosci. Biotechnol. Biochem.* **2010**, *74*, 2092–2095.
[17] a) R. H. Crabtree, *Acc. Chem. Res.* **1979**, *12*, 331–337; b) R. H. Crabtree, M. W. Davis, *J. Org. Chem.* **1986**, *51*, 2655–2661.
[18] a) H. Okamura, T. Iwagawa, M. Nakatani, *Tetrahedron Lett.* **1995**, *36*, 5939–5942; b) K. Afarinkia, V. Vinader, T. D. Nelson, G. H. Posner, *Tetrahedron* **1992**, *48*, 9111–9171.
[19] a) J. C. Anderson, A. J. Blake, J. P. Graham, C. Wilson, *Org. Biomol. Chem.* **2003**, *1*, 2877–2885; b) T. Sammakia, M. A. Berliner, *J. Org. Chem.* **1994**, *59*, 6890–6891; c) A. Alexakis, P. Mangeney, *Tetrahedron: Asymmetry* **1990**, *1*, 477–511.
[20] We have already explained the *exo* selectivity of this reaction by DFT calculation.[16a]
[21] R. J. Arhart, J. C. Martin, *J. Am. Chem. Soc.* **1972**, *94*, 5003–5010.
[22] a) G. M. Atkins, E. M. Burgess, *J. Am. Chem. Soc.* **1968**, *90*, 4744–4745; b) E. M. Burgess, H. R. Penton Jr., A. E. Taylor, *J. Am. Chem. Soc.* **1970**, *92*, 5224–5226; c) E. M. Burgess, H. R. Penton, E. A. Taylor, *J. Org. Chem.* **1973**, *38*, 26–31.
[23] L. Chugaev, *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3332–3335.
[24] H. W. Thompson, *J. Org. Chem.* **1971**, *36*, 2577–2581.
[25] S. Nara, H. Toshima, A. Ichihara, *Tetrahedron* **1997**, *53*, 9509–9524.

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